Persistence of Immune Response After MenACYW-TT Vaccination in Children, Adolescents, and Adults

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BACKGROUND

- *Neisseria meningitidis* is an important pathogen causing invasive diseases in all age groups. Invasive meningococcal diseases (IMD), including meningitis, septicemia, and purpura fulminans cause morbidity and mortality worldwide.
- At least three incidence peaks have been described, a first one in young children, a second peak in adolescents and young adults, and a third one in the older population (ie, adults ≥65 years of age).[1-3]
- Patterns of IMD across age groups and knowledge of immune persistence following meningococcal vaccination can inform strategies for meningococcal disease prevention and control.
- We present data regarding immune persistence at least 3 years after a priming dose of meningococcal quadrivalent conjugate vaccine (MenACYW-TT) in children; adolescents and young adults; and older adults compared to other meningococcal quadrivalent vaccines.

METHODS

- Three phase III randomized studies, 2 modified double blind (NCT03476135 and NCT04084769) and 1 open label (NCT04142242), included the assessment of immune persistence at least 3 years following primary vaccination in previous studies with either MenACYW-TT or a comparator meningococcal vaccine (MCV4-TT, MCV4-CRM or MPSV4) in children, adolescents and young adults, and older adults **(Table 1)**.
- A serum bactericidal assay with human complement (hSBA) was performed to determine seroprotection rates (SPRs; percentages of subjects with hSBA titers ≥1:8) and geometric mean titers (GMTs) against the four vaccine serogroups at 3 time points: before, 30 days after, and at least 3 years after primary vaccination.
- Descriptive statistics were provided for the hSBA antibody titers against meningococcal serogroups A, C, W, and Y. Percentages and GMTs were presented along with the relevant 95% confidence intervals.

Table 1. Studies providing immune persistence data

Study assessing the primary dose	Study country	Age group at primary dose	Vaccines used as primary dose	Study assessing antibody persistence*	Time interval between priming dose and antibody persistence assessment
MET54	Finland	Naïve toddlers 12-23 months	**MenACYW-TT** (MenQuadfi®) MCV4-TT (Nimenrix®)	**MET62**	3 years
MET50, MET43	USA, Puerto Rico	Naïve adolescents 10-17 years	**MenACYW-TT** (MenQuadfi®) MCV4-CRM (Menveo®)	**MET59**	3-6 years
MET49, MET44	USA	Naïve older adults ≥56 years	**MenACYW-TT** (MenQuadfi®) MPSV4 (Menomune®)	**MEQ00066**	3 years and 6-7 years

MenACYW-TT, MCV4-TT: Meningococcal quadrivalent conjugate (tetanus toxoid) vaccine. MCV4-CRM: Meningococcal quadrivalent conjugate (cross reacting material, non-toxic diphtheria) vaccine. MPSV4: Meningococcal quadrivalent polysaccharide vaccine

*Antibody persistence was measured prior to a booster dose of meningococcal quadrivalent vaccine

Clinical trials identifier: MET54: NCT03205358; MET50: NCT02199691; MET43: NCT02842853; MET44: NCT01732627; MET49: NCT02842866; **MET62: NCT03476135; MET59: NCT04084769; MEQ00066: NCT04142242**

RESULTS

- **Antibody persistence based upon seroprotection (hSBA titers ≥1:8) rates:** At least 3 years after primary vaccination, SPRs for serogroups C, W, and Y were generally higher in MenACYW-TT-vaccinated subjects vs those who received comparator meningococcal vaccines for all age groups **(Figures 1-3)**. In children, 3 years after priming, 100% of subjects met criteria for seroprotection as compared to those primed with MCV4-TT who had seroprotection rates of 57.1% for serogroup C, 89.8% for serogroup W, and 83.7% for serogroup Y. In older adults, 6-7 years after primary vaccination, SPRs declined in both MenACYW-TT- and MPSV4-primed participants; SPRs were similar or trended higher for MenACYW-TT-primed participants compared to those primed with MPSV4 for serogroups A, C, W, and Y **(Figure 4)**. The most substantial differences in SPRs were observed for serogroup C, while SPRs were generally similar between MenACYW-TT and comparator vaccines for serogroup A **(Figures 1 and 4)**.
- **Antibody persistence based upon GMTs:** Similarly, hSBA GMTs at least 3 years after a primary dose were higher for serogroups C, W, and Y in those vaccinated with MenACYW-TT vs comparator vaccines. The most substantial differences in GMTs were observed for serogroup C, while GMTs were generally similar between MenACYW-TT and comparator vaccines for serogroup A **(Figures 5-7)**. In older adults 6-7 years after vaccination, hSBA GMTs declined in both MenACYW-TT- and MPSV4-primed participants, with hSBA GMTs generally trending higher for MenACYW-TT- vs MPSV4-primed participants at this time point. Nevertheless, GMTs were generally higher than baseline levels prior to primary vaccination for serogroups C, W, and Y **(Figure 8)**.
- Overall, seroprotection rates and GMTs at least 3 years after a primary dose, remained higher than those seen prior to priming dose for all serogroups, and in all evaluated age groups, except for older adults for serogroup A, in which tended to be lower (SPR) or similar (GMTs).

Figure 1: Immune persistence: Seroprotection rates (hSBA ≥1:8) in children (MET62) 3y post-priming

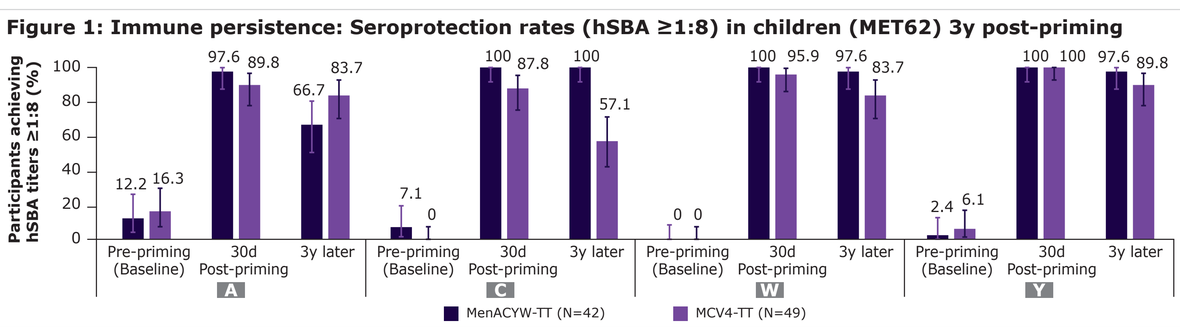


Figure 2: Immune persistence: Seroprotection rates (hSBA ≥1:8) in adolescents & young adults (MET59) 3-6y post-priming

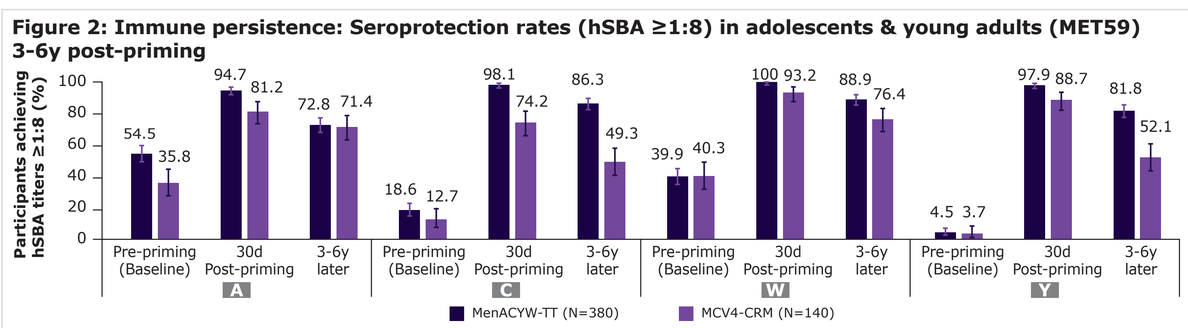


Figure 3: Immune persistence: Seroprotection rates (hSBA ≥1:8) in older adults (MEQ00066) 3y post-priming

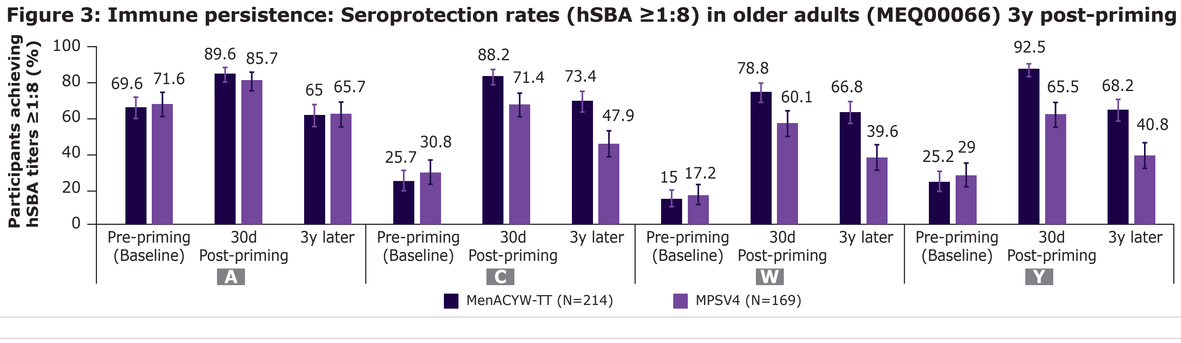


Figure 4: Immune persistence: Seroprotection rates (hSBA ≥1:8) in older adults (MEQ00066) 6-7y post-priming

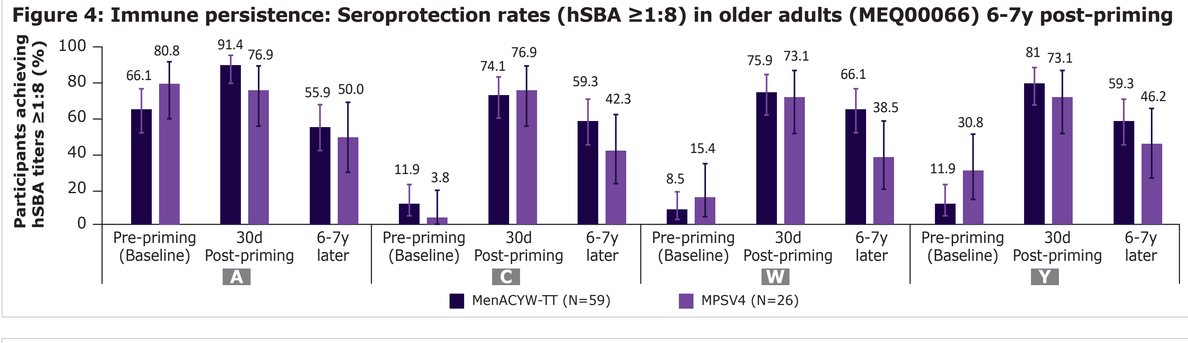


Figure 5: Immune persistence: hSBA GMTs in children (MET62) 3y post-priming

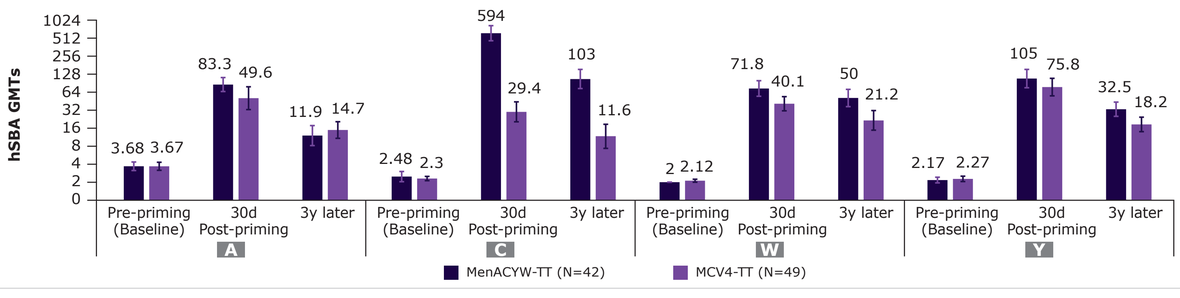


Figure 6: Immune persistence: hSBA GMTs in adolescents & young adults (MET59) 3-6y post-priming

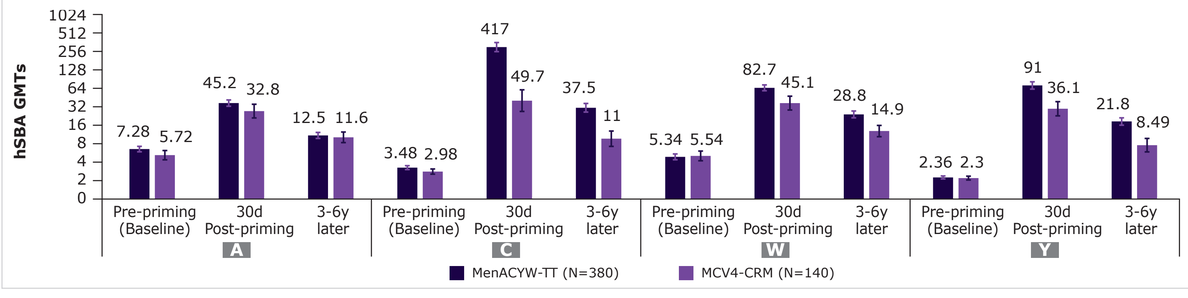


Figure 7: Immune persistence: hSBA GMTs in older adults (MEQ00066) 3y post-priming

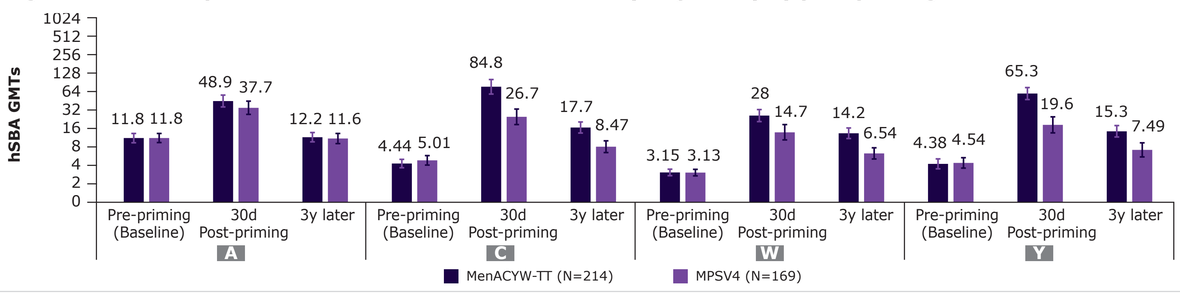
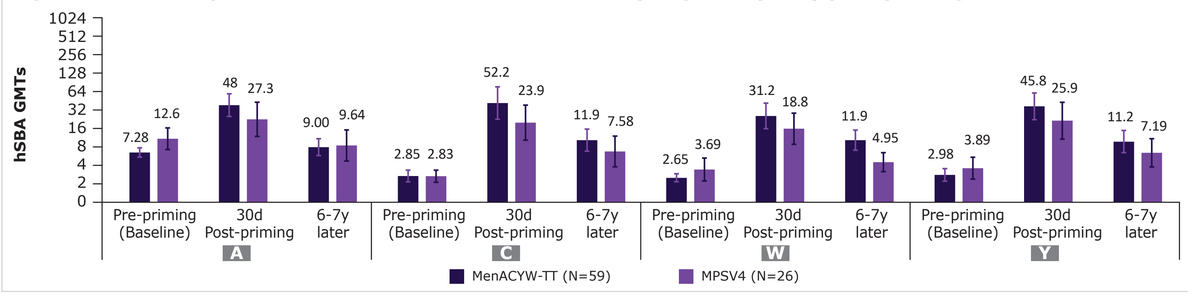


Figure 8: Immune persistence: hSBA GMTs in older adults (MEQ00066) 6-7y post-priming



d: day. GMT: geometric mean titer. hSBA, serum bactericidal assay with human complement. MenACYW-TT, MCV4-TT: Meningococcal quadrivalent conjugate (tetanus toxoid) vaccine. MCV4-CRM: Meningococcal quadrivalent conjugate (cross reacting material, non-toxic diphtheria) vaccine. MPSV4: Meningococcal quadrivalent polysaccharide vaccine. y: year

CONCLUSIONS

- MenACYW-TT induced consistently higher antibody persistence as assessed by seroprotection (hSBA titers ≥1:8) rates and GMTs vs comparator vaccines for serogroups C, W, and Y at least 3 years after primary vaccination in toddlers, adolescents and young adults, and older adults, indicative of long-term persistence of the immune response.
- These data may provide support for decisions around the use of meningococcal vaccines for the prevention of IMD in persons 12 months of age and older.

REFERENCES

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3. Cohn AC et al. Clin Infect Dis. 2010 Jan 15;50(2):184-91.

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DISCLOSURE OF CONFLICTS

- BZ, CR, KG, SB and MD are employees of Sanofi and may hold company shares and/or stock options. JP, MV and JJ received funds to their institutions from Sanofi to cover the costs of performing the study.

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